PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference JE/P/242/WOD	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/GB2004/004442	International filing date *(day/month/year)* 21.10.2004	Priority date *(day/month/year)* 21.10.2003
International Patent Classification (IPC) or national classification and IPC A61K9/18, A61P35/00		
Applicant PSIMEDICA LIMITED et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
11.08.2005	01.02.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Vermeulen, S Telephone No. +49 89 2399-7520

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/004442

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-26 as originally filed

   Claims, Numbers

   1-21 as originally filed

   Drawings, Sheets

   1/8-8/8 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 11-15,17-21

because:

☒ the said international application, or the said claims Nos. 11-14,17-21 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 15

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☒ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
   - ☐ complied with.
   - ☒ not complied with for the following reasons:

     see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
   - ☐ all parts.
   - ☒ the parts relating to claims Nos. 1-14,16-21 .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14,16-21
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-12,21
	No:	Claims	13,14,16-20
Industrial applicability (IA)	Yes:	Claims	1-10,16
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 11-14 and 17-21 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT).

Re Item IV

Lack of unity of invention

The present set of claims comprises two inventions which are not so linked as to form a single general inventive concept (Rule 13.1 PCT), because the groups of claims do not have common or corresponding special technical features making a possible contribution over the state of the art. In the present application the two groups of claims represent solutions to different technical problems:

Claims 1-14 and 16-21: improved cancer treatment by combining a cytotoxic drug with a porous carrier material.

Claim 15: use of a specific cytotoxic drug in chemo-brachytherapy.

The present report has been drawn up for the first group of claims.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following document/s/:

D1: WO 02/067998 A (PSIMEDICA LIMITED; CANHAM, LEIGH, TREVOR; ASTON,

ROGER) 6 September 2002 (2002-09-06)

D2: WO 02/15881 A (DYTECH CORPORATION LTD; SAMBROOK, RODNEY, MARTIN; AUSTIN, WAYNE; SAMBR) 28 February 2002 (2002-02-28)

D3: US-A-4 873 092 (AZUMA ET AL) 10 October 1989 (1989-10-10)

D4: DE 38 41 397 A1 (MELZER, WOLFGANG, DR., 8000 MUENCHEN, DE) 21 June 1990 (1990-06-21)

2. The present independent claims 1, 10, 11, 13, 16, 17 and 18 relate to the use of an extremely large number of possible porous carrier materials. Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of porous carrier materials. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search and examination over the whole of the claimed scope is impossible. Consequently, the search has been carried out and the present opinion established for those porous carrier materials which appear to be supported and disclosed (cf. description and examples), i.e. semi-conductors such as silicon, germanium, silicon carbide or silicon nitride (cf. claim 2).

3. The use according to independent claim 13 does not involve an inventive step (Art.33(3) PCT) in view of prior art teaching which can be taken from D1-D4.

3.1 D1 discloses the use of porous silicon particles for local delivery of cytotoxic drugs into an organ in which a tumour is located in such a manner as to optimise the therapeutic effect of the cytotoxic drug, while minimizing adverse systemic side effects.

3.2 Similarly, D2 discloses the use of porous carriers, such as silicon carbide, for site specific and controlled anti-cancer drug delivery with low frequency of systemic side effects.

3.3 Hence, no inventive step can be seen in the use according to claim 13, since upon reading D1 and D2 it is obvious to the skilled person that slow local release of

cytotoxic drugs by a carrier material may allow loading of higher doses as compared to direct administration of the toxic drug without carrier material. This becomes also apparent from the teaching e.g. of D3 and D4 (cf. passages cited in the ISR).

4. The use as defined in the independent claims 16, 17 and 18 also does not involve an inventive step (Article 33(3) PCT) in view of prior art teaching which can be taken from D1.

4.1 D1 discloses teaches to use of porous silicon microparticles or implants as carrier material for the delivery of cytotoxic drug in the treatment of cancer by chemo-brachytherapy. Although in D1 the impregnation of porous silicon is not explicitly exemplified for paclitaxel or chlorambucil, said document clearly suggests the impregnation with several types of cytotoxic drugs, such as alkylating agents, cytotoxic antibodies, antimetabolites, vinca alkaloids and hormonal regulators.

4.2 Hence, no inventive step can be seen in the restriction to the presently claimed cytotoxic drugs, since they are an obvious alternative which the skilled person would consider, upon reading D1.

5. In view of the state of the art disclosed in D1-D4, also the dependent claims 14, 19 and 20 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, would render the claimed subject-matter novel and/or inventive (Art.33(2)-(3) PCT). The specific embodiments are known or at least suggested by the cited state of the art. None of the claimed features appears to bring a solution to any specific problem, as compared to the state of the art, which solution would involve an inventive step.

6. The use according to claims 1-12 and 21 is considered novel and inventive (Art. 33(2)(3) PCT), because none of the cited prior art documents discloses the intra-tumoural administration of a composition comprising a cytotoxic drug and a porous carrier material as defined in the present application.

7. The use as defined in claims 1-10 and 16 is considered to be industrially applicable and accordingly meets the requirements of Art.33(4) PCT.